Regulated expansion of human pancreatic beta-cells.

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Public Summary:
Although pancreatic beta-cell transplantation may serve as a potential cure for diabetes mellitus (DM), limited donor tissue availability poses a major challenge. Thus, there is a great demand to find new sources for pancreatic beta-cells. Here, we present a lentiviral vector-based approach to achieve beta-cell proliferation through the beta-cell-specific activation of the hepatocyte growth factor (HGF)/cmet signaling pathway. The methodology is based on the beta-cell-specific expression of a ligand-inducible, chimeric receptor (F36Vcmet), under transcriptional control of the promoter from the human insulin gene, and its ability to induce HGF/cmet signaling in the presence of a synthetic ligand (AP20187). High transduction efficiency of human pancreatic islets was achieved utilizing this approach with chimeric receptor expression confined to the beta-cell population. In addition, specific proliferation of human pancreatic beta-cells was induced utilizing this approach. Selective, regulated beta-cell expansion may help to provide greater availability of cells for transplantation in patients with DM.

Scientific Abstract:
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